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A Review on Advanced Transdermal Paches and Their Evaluation

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ABSTRACT

Transdermal patches are an innovative method of delivering medication directly into the bloodstream through the skin. In 1979, the United States authorized the use of the initial transdermal technique for systemic delivery—a three-day patch that administers scopolamine to alleviate motion sickness. The initial breakthrough in transdermal delivery came with the introduction of nicotine patches. This paved the way for greater awareness and acceptance of transdermal technology in the medical field and among the general population, gaining significant popularity a decade later. Currently, there are 19 different transdermal delivery methods available for medications such as oestradiol, fentanyl, lidocaine, and testosterone. Additionally, there are combination patches available that contain multiple medications for hormone replacement and contraception. There are also iontophoretic and ultrasonic analgesia delivery systems that can be used. They provide several benefits compared to conventional oral medication, such as improved patient adherence, regulated drug delivery, and reduced side effects. The medication is typically contained within a matrix or reservoir within the patch, and is gradually released over a period of time. The patch may require periodic changes, typically every few days or weeks, depending on the specific medication and dosage. Transdermal patches have a broad range of applications, encompassing painkillers, hormones, and nicotine replacement therapy. They are widely regarded as safe and effective, with minimal side effects. It is important to carefully adhere to the instructions for use to avoid potential skin irritation or other issues.

Keywords: Skin absorption, Medication convenience, Gastrointestinal side effects, Drug interactions.

INTRODUCTION

Transdermal patches are a type of medical device that delivers medication through the skin and into the bloodstream. They are designed to provide a convenient and steady delivery of medication over an extended period of time, and are often used as an alternative to oral medications or injections.[1]

Transdermal patches are typically made up of several layers, including a backing layer, an adhesive layer, a drug layer, and a release liner. The drug layer contains the medication, which is usually embedded in a matrix or reservoir that slowly releases the medication over time. The adhesive layer helps the patch stick to the skin, while the backing layer protects the medication from the outside environment.[2-4]

It can be used to deliver a wide range of medications, including painkillers, hormones, and nicotine replacement therapy. They are generally considered safe and effective, with few side effects. However, it is important to follow the instructions for use carefully, as improper use can lead to skin irritation or other problems. They have several advantages over other methods of drug delivery. They can provide a more constant blood concentration of the medication, which can lead to better therapeutic outcomes. They can also be more convenient for patients who have difficulty swallowing pills or who require frequent dosing. Additionally, transdermal patches can reduce the

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risk of gastrointestinal side effects and drug interactions that may occur with oral medications. Overall, transdermal patches are a useful and effective method of drug delivery for many medications. They can provide a convenient, steady, and safe way to deliver medication to patients, and may be particularly beneficial for those who have difficulty taking medications orally or who need constant drug delivery over an extended period of time.[5-6]

Physiology of Skin

A typical adult's skin has a surface area of around $2m^2$, and it gets about one-third of the blood that circulates through the body. Skin contains highest stratum corneum of the epidermis, which is composed of highly cornified (dead) cells embedded in a continuous matrix of lipid membranous sheets, is divided into four morphologically distinct regions: the basal layer, spiny layer, stratum granulosum, and uppermost stratum corneum. Ceramides, cholesterol, and free fatty acids make up the special composition of these extracellular membranes. Every square centimetre of human skin is known to have between 200 and 250 sweat ducts and 10 to 70 hair follicles on average. It is one of the human most readily accessible organs of human.[7-10]

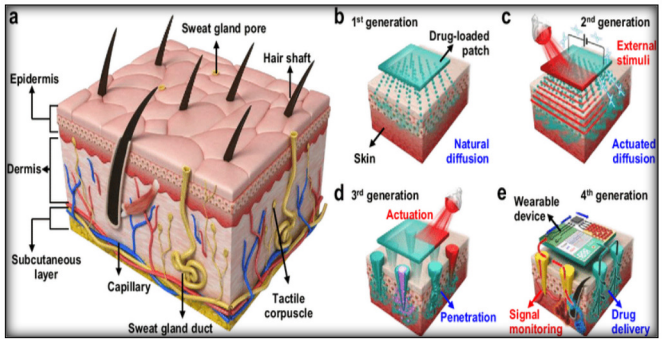

Figure 1: Structure of Skin

Skin Pathways for Transdermal Patches:

When drugs are applied on the skin surface, penetration into and through the skin can occur via various routes. Drugs penetrate either via the stratum corneum or via the appendages. During penetration through the stratum corneum, two possible routes can be distinguished, Penetration alternating through the corneocytes and the lipid lamellae and Penetration along the tortuous pathway along the intercellular route.

Generally, it is accepted that the predominant route of penetration through the stratum corneum is the intercellular route. This is mainly caused by the densely cross-linked cornified envelope coating the keratinocytes. However transcellular transport for small hydrophilic molecules such as water cannot completely be excluded. The appendage route or shunt route includes either the duct of the eccrine sweat glands or the follicular duct. The content of the eccrine sweat glands is mainly hydrophilic, while the content of the follicular duct is lipophilic. This is mainly due to the sebum excreted into the opening of the follicular duct. It is generally accepted that due to its large surface area, passive skin permeation mainly occurs through intact stratum corneum.

Transdermal patches are also a preferred option for medications that have a short halflife and require frequent dosing, as they can provide a sustained release of medication over a longer period of time. This can help to improve patient compliance and reduce the risk of missed doses, which can lead to suboptimal treatment outcomes.

In addition to their therapeutic benefits, transdermal patches offer several practical advantages for both patients and healthcare providers. They are easy to use and do not require any special training or equipment, making them a convenient option for self-administration. They also eliminate the need for frequent injections or visits to the doctor's office, which can reduce the burden on patients and healthcare systems.[11-13]

Despite their many advantages, transdermal patches are not suitable for all medications. Some drugs may not be able to penetrate the skin or may cause skin irritation or other adverse effects. Additionally, the patches must be designed to release the medication at a consistent rate, which can be challenging for some drugs. Overall, transdermal patches are a valuable tool for drug delivery that offer several benefits over other methods of administration. They can provide a convenient and safe way to deliver medication to patients, while also improving therapeutic

outcomes and reducing the burden on healthcare systems.[15-16]

To ensure the safe and effective use of transdermal patches, it is important for healthcare providers to carefully select the appropriate medication and patch for each patient's individual needs. This may involve considering factors such as the patient's age, weight, medical history, and other medications they are taking. Patients using transdermal patches should also be instructed on proper use and care of the patch, including how often to change it and how to dispose of used patches. They should be advised to avoid exposing the patch to water or excessive heat, as this can affect the integrity of the patch and reduce its effectiveness.[17]

Figure 2: Application and absorption layers of transdermal patches

Advantages of Transdermal Patches

Transdermal patches offer several advantages over other methods of drug delivery, including:

Consistent delivery: Transdermal patches provide a steady and consistent release of medication over an extended period of time. This can lead to more stable blood concentrations of the medication and improved therapeutic outcomes.

Convenience: Transdermal patches are easy to use and do not require any special training or equipment. They can be applied by patients themselves and do not require frequent injections or visits to the doctor's office.

Reduced side effects: Transdermal patches can reduce the risk of gastrointestinal side effects that may occur with oral medications. They also avoid the first-pass metabolism effect in the liver, which can reduce the risk of drug interactions.

Improved compliance: Transdermal patches can provide a more convenient and less burdensome way for patients to receive their medication, which can lead to improved compliance and treatment outcomes.

Customizable dosing: Transdermal patches can be designed to release medication at a specific rate, which can be customized to meet the individual needs of each patient.

Prolonged release: Transdermal patches can provide a sustained release of medication over a longer period of time, which can be particularly beneficial for medications that have a short half-life and require frequent dosing.[18-20]

Disadvantages of Transdermal Patches

While transdermal patches offer several advantages, there are also some disadvantages that should be considered. These include:

Limited drug options: Not all medications are suitable for transdermal delivery. Some drugs may not be able to penetrate the skin, or may cause skin irritation or other adverse effects.

Slow onset of action: Transdermal patches may have a slower onset of action compared to other methods of drug delivery. This can be problematic for medications that require rapid relief of symptoms.

Skin irritation: Some patients may experience skin irritation or other adverse effects from the patch adhesive or medication. This can be particularly problematic for patients with sensitive skin.

Inconsistent absorption: The rate of drug absorption through the skin can vary depending on factors such as skin type, temperature, and humidity. This can lead to inconsistent drug levels in the blood and reduced therapeutic effectiveness.

Dosing limitations: The amount of medication that can be delivered through a transdermal patch is limited by the size of the patch and the concentration of the medication. This can be

problematic for medications that require high doses or rapid titration.

Cost: Transdermal patches can be more expensive than other methods of drug delivery, particularly for medications that require frequent dosing or large patch sizes.[21-24]

Types of Transdermal Patches[25-28]

Transdermal patches can be classified into four categories:

Reservoir patches:

Reservoir patches are a type of transdermal patch that use a reservoir or cavity to hold the medication. The reservoir is typically made of a semi-permeable membrane that allows the medication to pass through but prevents water and other substances from entering.

The medication is contained in a gel or liquid form within the reservoir, and a rate controlling membrane controls the release of the medication into the skin. This membrane is usually made of a polymer or adhesive material that can be designed to release the medication at a specific rate.

Reservoir patches can be designed to release medication for an extended period of time, ranging from a few hours to several days. They can be used to deliver a wide range of medications, including hormones, analgesics, and cardiovascular drugs.

Matrix patches:

Matrix patches are a type of transdermal patch that use a matrix or adhesive layer to hold the medication. The medication is dispersed or dissolved within the adhesive layer, and a rate-controlling membrane controls the release of the medication into the skin.

The adhesive layer is typically made of a polymer material that can be designed to release the medication at a specific rate. The medication can be dispersed throughout the entire adhesive layer or can be localized to a specific area within the patch.

Matrix patches can be designed to release medication for an extended period of time, ranging from a few hours to several days. They can be used to deliver a wide range of medications, including nicotine, pain medications, and hormone therapies.

Micro-reservoir patches:

Micro-reservoir patches are a type of transdermal patch that use small micro reservoirs to hold the medication. These micro-reservoirs are typically made of a polymer material and are embedded within the adhesive layer of the patch.

The medication is contained within the micro-reservoirs, which are designed to release the medication at a controlled rate. The size and number of micro reservoirs can be customized to meet the specific needs of each medication and patient.

Micro-reservoir patches can provide a more precise and controlled release of medication compared to other types of transdermal patches. They can be used to deliver a wide range of medications, including vaccines, peptides, and proteins.

Adhesive patches:

Adhesive patches are a type of transdermal patch that use an adhesive layer to hold the medication. The medication is typically dissolved or dispersed within the adhesive layer, and a rate-controlling membrane controls the release of the medication into the skin.

The adhesive layer is designed to adhere to the skin and can be made of a variety of materials, such as acrylics or silicones. The medication can be dispersed throughout the entire adhesive layer or can be localized to a specific area within the patch.

Adhesive patches can be used to deliver a wide range of medications, including nicotine, pain medications, and hormone therapies. They can be designed to release medication for an extended period of time, ranging from a few hours to several days.[29-32]

Components of Transdermal Patches:

Transdermal patches typically consist of several components, including:

Backing layer: This is the outermost layer of the patch and is typically made of a flexible material such as polyester or polyethylene. The backing layer protects the patch from external factors such as moisture and helps to maintain the structural integrity of the patch.

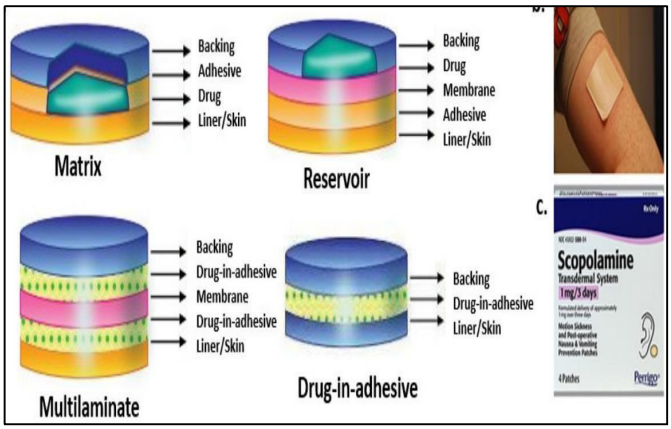

Figure 3: Types of Transdermal patches

Adhesive layer: This layer is responsible for adhering the patch to the skin. The adhesive layer is typically made of a polymer material, such as acrylic or silicone, and may contain the medication.

Rate-controlling membrane: This layer is responsible for controlling the rate at which the medication is released from the patch. The membrane is typically made of a polymer material and can be designed to release the medication at a predetermined rate over a specific time period.

Medication reservoir: Some transdermal patches contain a reservoir that holds the medication. The reservoir can be made of a variety of materials, such as a gel or a solid matrix, and is typically placed between the rate controlling membrane and the adhesive layer.

Release liner: This is a protective layer that is removed before the patch is applied to the skin. The release liner is typically made of a silicone-coated material that prevents the adhesive layer from sticking to other surfaces. It is made up of base layer which may be Non-occlusive and Occlusive.

Optional components: Some transdermal patches may also contain additional components, such as a protective layer that covers the medication reservoir, or an the enhancer layer that helps to increase the skin's ability to absorb medicines.

specific components and design of a transdermal patch can vary depending on the being medication delivered and the desired release profile. Careful consideration should be given to the selection of materials and design to ensure safe and effective use of the patch.[33-35]

Drug: Transdermal drug administration refers to substances that are absorbed through the skin layers.[36] To be delivered trans-dermally, an ideal drug should have following properties:

Ideal properties of drug:

Table 1: Ideal properties of drug[37-41]

Parameter	Properties
Dose	Should be low in weight (less than 20mg/day)
Half- life	10/less (hrs)
Molecular weight	<400 Dalton
Skin permeability coefficient	>0.5*10-3cm/h.
Skin Reaction	Non irritating, Non sensitizing
Oral bioavailability	Low.

Table 2: Factors Affecting Formulation of TDDS[42-44]

Physicochemical	Pharmacokinetic	Biological
Solubility	Half life	Skin toxicity
Crystalinity	Volume of distribution	Site of application
Molecularity	Total body clean	Allergic Reaction
Polarity	Therapeutic plasma concentration	Skin metabolism
Melting point	Bioavailable factor	_____

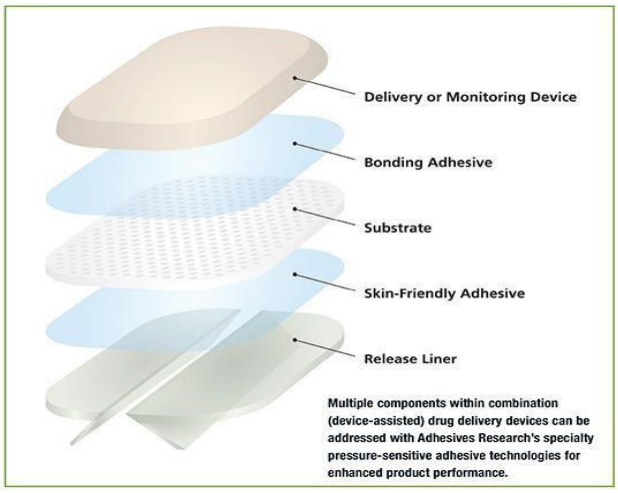

Figure 4: layers of polymers[45]

Polymers Used in Transdermal Patches:

There are several types of polymers that can be used in the formulation of transdermal patches. Some common examples include:

Acrylic polymers: These are often used as the matrix in matrix-type transdermal patches. They are known for their ability to provide a sustained release of the drug.

Cellulose derivatives: These polymers are often used as the membrane layer in transdermal patches. They can be designed to control the rate of drug release and increase the permeability of the skin.

Silicone-based polymers: These polymers are often used in transdermal patches because of their biocompatibility and ability to provide a sustained release of the drug.

Polyurethane: This is a versatile polymer that can be used in both the matrix and membrane layers of transdermal patches. It can provide a sustained release of the drug and can be designed to be permeable or non-permeable.

Ethylene-vinyl acetate (EVA): This is a polymer that can be used as the matrix in matrix-type transdermal patches. It is known for its ability to provide a controlled release of the drug.

The choice of polymer will depend on a number of factors, including the desired release profile of the drug, the compatibility of the polymer with the drug, and the biocompatibility of the polymer with the skin.[46-48]

Preparation of Transdermal Patches[49-50]

There are several methods used for the manufacture of transdermal patches. Some of the common methods include:

Solvent casting: In this method, the medication is dissolved or dispersed in a solvent, and the solution is then cast onto a backing layer to form the adhesive layer. The rate-controlling membrane is then applied on top of the adhesive layer, and the release liner is added.

Hot melt extrusion: This method involves melting the medication and the adhesive together, and extruding the mixture through a die to form a solid matrix. The matrix is then cut to size and the release liner is added.

Lamination: In this method, the adhesive layer, rate-controlling membrane, and backing layer are each separately produced, and then laminated together to form the patch.

Spray coating: In this method, the medication is dissolved or dispersed in a solvent, and the solution is then sprayed onto the backing layer to form the adhesive layer. The rate-controlling membrane and release liner are then added.

Asymmetric TPX membrane method: A prototype patch may be made for this using a heat sealable polyester film (type 1009, 3m) with a backing membrane that has a concave of 1 cm in diameter. A poly (4-methyl-1pentene) asymmetric membrane made of TPX is used to cover the concave membrane, which is then sealed with an adhesive. Preparation of an asymmetric TPX membrane These are made utilising a procedure called dry/wet inversion. To create a polymer solution, TPX is dissolved in cyclohexane, a solvent, and nonsolvent additives. With a Gardner knife, the polymer solution is cast onto a glass plate at a predetermined thickness after being maintained at 40°C for 24 hours. After that the a casting film is evaporated at 50°C for 30 sec, then the glass plate is to be immersed immediately in coagulation bath [maintained the temperature at 25°C]. After 10 minutes of immersion, the

membrane can be removed, air dry in a circulation oven at 50°C for 12 hrs.[51-52]

Circular Teflon mould method: Solutions with different ratios of polymers are utilised in an organic solvent. Half as much of the same organic solvent is used to dissolve the calculated amount of medication. The second half of the organic solvent is used to dissolve enhancers at various concentrations before they are applied. Di-N-butyl phthalate, a sticky substance, will be dissolved in the medication solution. Aluminium foil is used to line a specially constructed aluminium former, and precisely fitted cork blocks are used to seal off the ends.

Mercury substrate method: In this procedure, the plasticizer and medication are dissolved in a polymer solution. To prevent solvent evaporation, cover the mercury surface with an inverted funnel after stirring the aforementioned solution for 10 to 15 minutes to ensure a homogeneous dispersion.

Drugs Used in Tansdermal Patches:

Table 3: Drugs used in transdermal patches[53]

Drug	Indication	Patch Design	Site of Application	Duration of Application
Buprenorphine	Chronic pain	DIA	arm, upper chest, upper back or the side of the chest	7 days
Clonidine	Hypertension	Reservoir / Membrane	Upper outer arm or upper	7 days
Scopolamine	Motion	Reservoir/ membrane	Behind one ear	72 hrs
Methyl salicylate	Muscles and joint pain	DIA	The affected area	Up to 8-12 hrs
Selegiline	Major depressive disorder	DIA	Upper chest, upper thigh or the outer surface of the upper arm	24 hrs
Nicotine	Smoking cessation	Matrix	Upper body or the outer part of the arm	24 hrs
Sumatriptan	Migraine	Iontophoretic system	Upper arm or thigh	4 hrs
Capsaicin	Neuropathic pain	DIA	The most painful area, excluding and scalp	Single 60 min application of up to four
Testosterone	Hypogonadism	Reservoir / membrane	Back abdomen, thighs or upper arm	24 hrs

Evaluation Parameters[48-51]

Thickness of the patch: Thickness of the patch: The thickness of the drug loaded patch is measured in different points by using a digital micrometer and the average thickness and standard deviation is determined to ensure the thickness of the prepared patch. The thickness of transdermal film is determined by travelling microscope dial gauge, screw gauge or micrometer at different points of the film.

Weight uniformity: Prior to testing, the produced patches are dried at 60°c for 4 hours. A predetermined patch area must be divided into various patches and weighed using a digital balance. From the individual weights, the average weight and standard deviation values should be computed.

Folding endurance: A strip of specific area is to be cut evenly and repeatedly folded at the same place till it breaks. The number of times the film could be folded at the same place without breaking gives the value of the folding endurance.

Percentage Moisture content: The prepared films are to be weighed individually and to be kept in a desiccator containing fused calcium chloride at room temperature for 24 hrs. After 24 hrs the films are to be reweighed and determine the percentage moisture content from the below mentioned formula 2, 13.

% Moisture content = Initial weight – Final weight /Final weight. X 100

Content uniformity: test A total of 10 patches are chosen, and each patch's content is chosen. Transdermal patches pass the content uniformity test if, out of ten patches, nine have content between 85% and 115% of the given value and one has content between 75% and 125% of the specified value. The drug content of an additional 20 patches is examined, though, if 3 patches have content between 75% and 125%. The transdermal patches pass the test if these 20 patches have a range of 85% to 115%.

Moisture Uptake: Films that have been weighed are maintained in desiccators for 24 hours at room temperature. These are then removed and dried in desiccators using saturated potassium chloride solution at 84% relative humidity until a consistent weight is reached. The formula for percentage moisture uptake is shown below.

% moisture uptake = Final weight - Initial weight/Initial weight X 100

Drug content: In an appropriate solvent, a predetermined patch area must dissolve in a predetermined volume. After that, the solution must be filtered through a filter medium so that the drug content may be determined using the appropriate technique (UV or HPLC). Each number is the average of three distinct samples.

Procedure for The Application of Transdermal Patches[53]

Transdermal patches are applied to the skin to deliver medication into the bloodstream through the skin. Here are the general steps for applying a transdermal patch:

Clean the skin: Start by cleaning the area of skin where you plan to apply the patch. Use mild soap and water to cleanse the skin, and pat it dry with a clean towel. Avoid using any lotion, oil, or other products on the skin, as they may interfere with the patch's adherence.

Remove the patch from its packaging: Carefully peel the patch from its protective backing, being careful not to touch the adhesive surface with your fingers. Most patches have a protective cover that you will need to remove before applying the patch.

Apply the patch: Place the adhesive side of the patch onto the clean, dry skin. Press firmly with your fingers or the palm of your hand to make sure the patch adheres well to the skin. Make sure the patch is applied flat and smooth without any wrinkles or folds.

Dispose of used patches properly: After the recommended wear time (usually 24 hours or as instructed by your healthcare provider), carefully remove the used patch from the skin. Fold it in half with the adhesive sides together, and dispose of it properly according to local regulations.

Rotate patch placement: If needed to apply multiple patches, make sure to rotate the application sites to avoid skin irritation. Do not apply a new patch to the same spot for consecutive applications.

CONCLUSION

In conclusion, transdermal patches are a convenient and effective way to deliver medication through the skin and into the bloodstream. They can provide a controlled release of medication over a period of time, avoiding the need for frequent dosing.

Formulating a transdermal patch involves selecting the appropriate drug and designing a patch that can deliver the drug in a controlled and consistent manner. Application of the patch requires careful attention to cleaning and placement to ensure optimal adherence and drug delivery.

Transdermal patches can offer a number of benefits, such as improved patient compliance, reduced side effects, and consistent medication delivery. However, they may not be suitable for all medications or patients.

The highly accomplished scientists all over the world are utilizing their potential role in controlled release. Transdermal delivery is a remarkably efficient mode of administration if a medicine has the proper balance of physical chemistry and pharmacology. The core elements of a transdermal patch, such as drug reservoirs, liners, adherents, permeation enhancers, backing laminates, plasticizers, and solvents, are crucial to the drug's release through the skin.

The pharmaceutical industry has many benefits and drawbacks related to drugs, and it is crucial that they are objectively included into the pharmaceutical production process so that the benefits can be felt in patient healthcare in the very near future.

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REFERENCE

1. Prausnitz MR, Langer R. Transdermal drug delivery. Nat Biotechnol. 2008; 26(11):1261-1268.
2. Hadgraft J. Transdermal drug delivery: 200 years of progress. J Pharm Sci. 2019;108(6):2083-2094.
3. Sivaraman G, Kumaraswamy M. Transdermal drug delivery system: an overview. Int J Pharm Sci Res. 2013;4(6):1997-2008.
4. Sampath Kumar KP, Debjit Bhowmik and Chiranjib B, R M Chandira. A review-Transdermal Drug Delivery System - A Novel Drug Delivery System and its market scope and opportunities. International Journal of Pharma and Bio Sciences, 2010, 1(2),1-21
5. Jain NK. Advances in controlled and novel drug delivery, 1st Ed., CBS Publishers and distributors, New Delhi .2001; 108-110
6. Barry BW, William AC. In: Swarbrick J(ed)) Boylon JC.Encyclopedia of pharmaceutical technology vol-II, Marcel Dekker: Inc New York, 1995, 49-93.
7. Tanner T, Marks R.Delivering Drugs by the Transdermal Route: review and comment. Skin Research and Technology, 14, 2008, 249-260.
8. Saltzman W, Mark Torchilin, Vladimir P. Drug delivery systems, Access Science, McGraw-Hill Companies, 5(2), 2008, 125-136
9. Sharma Teja, Rawal Gaurav, Transdermal Therapeutic Systems, An overview, International Journal of Pharmaceutical & Biological Archives, 2011, 2(6),15811587.
10. Wiechers J, Use of Chemical Penetration Enhancers in Transdermal Drug Delivery-Possibilities and Difficulties, Acta Pharm, 1992, 4, 123.
11. Manvi F.V, Dandagi P.M, Gadad A.P, Mastiholimat V.S and Jagdeesh T, Formulation of Transdermal Drug Delivery System of Ketotifen Fumarate, IJPS, 2003, 65(3), 239-243.
12. Kanikkannan N, Jayaswal S.B and Singh J, Transdermal Delivery of Indomethacin: Release Profile of Drug from Polymeric Patches, Indian Drugs, 30(9), 441-445.
13. Sankar V, Velrajan G, Palaniappan R and Rajasekar S, Design and Evaluation of Nifedipine Transdermal Patches, IJPS, 2003, 65(5), 510-515.
14. Ryan F, Donnelly, Paul A, McCarron, Design and Physicochemical Characterization of a Bioadhesive Patch for Dose-Controlled Topical Delivery of Imiquimod, International Journal of Pharmaceutics, 2006, 307,318-325.
15. Hemangi J, Patel, Jitendra S, Patel, Keyur D, Patel, Transdermal Patch for Ketotifen Fumarate as Asthmatic Drug, IJPR, 2009,l(1),1297-1304. 28.
16. Shalu Rani, Kamal Saroha, Navneet Syan, Transdermal Patches a successful tool in Transdermal Drug Delivery System: An overview, Der Pharmacia Sinica, 2011, 2 (5),17-29.
17. Azhar Ahmed, Nirmal Karki, Rita Charde, Manoj Charde, Bhushan Gandhare, Transdermal Drug Delivery Systems, An overview, International Journal of Biomedical and Advance Research, 2011, 02(01),38-56.
18. Parthasarathy G, Bhaskar reddy K and Prasanth V.V, Formulation and Characterization of Transdermal Patches of Naproxen with various polymers, International

Journal of Comprehensive Pharmacy , 2011, 6 (07), 1-3.

19. Kavitha K and More Mangesh Rajendra, Design and Evaluation of Transdermal Films of Lornoxicam, IJPBS, 2011, 2(2), 54-62.
20. Shalu Rani, Kamal Saroha, Navneet Syan, Pooja Mathur, Transdermal Patches A Successful Tool In Transdermal Drug Delivery System: An overview, Der Pharmacia Sinica, 2011, 2 (5), 17-29.
21. Kamal Saroha, Bhavna Yadav, Benika Sharma, Transdermal Patch, A Discrete Dosage Form, International Journal of Current Pharma Research, 2011,3(3), 98108.
22. Shah S, Transdermal Drug Delivery Technology Revisited, Recent Advances, Pharmainfo Net, 2008, 6(5),
23. Prabhu Prabhakara, Marina Koland, Preparation and Evaluation of Transdermal Patches of Papaverine Hydrochloride, International Journal of Research Pharmaceutical Sciences, 2010,1(3), 259-266.
24. Kulkarni V.H, Keshavayya J, Transdermal Delivery of Terbutaline sulphate through modified Chitosan membrane, Indian Journal of Pharmaceutical Education, 2004, 38(4), 189- 190.
25. Mutalik, N, Udupa, Glibenclamide Transdermal Patches, Physicochemical, Pharmacodynamic and Pharmacokinetic Evaluations, Journal of Pharmaceutical Sciences, 2004, 93 (6), 1557-1594.
26. Pravin Gavali, Atul, Gaikwad, Radhika P.R, Sivakumar T, Design and Development of Hydroxypropyl Methylcellulose based polymeric film of Enalapril Maleate, International Journal Of Pharmtech Research, 2010, 2(1), 274282.
27. Basavaraj K, Nanjwade, Kiran Suryadevara, Kella M.R and Sai Susmitha, Formulation and Evaluation of Transdermal Patches of Ondansetron Hydrochloride using various polymers in different ratios, Current Trends In Biotechnology and Pharmacy, 2010, 4 (4), 917-921.
28. Janos Bajdik, Geza Regdon JR, The effect of the solvent on the film-forming parameters of Hydroxypropyl-cellulose, International Journal of Pharmaceutics, 2005, 301, 192-198.
29. Koteshwar K.B, Udupa N and Vasantha Kumar, Design and Evaluation of Captopril Transdermal Preparations, Indian Drugs, 15 (29), 680-685.
30. Priyanka Arora, Biswajit Mukherjee, Design Development Physicochemical and in-vitro Evaluation of Transdermal Patches Containing Diclofenac Diethylammonium Salt, Journal of Pharmaceutical Sciences, 2002, 91(9), 20762089.
31. Sankar V, Velrajan G, Palaniappan R and Rajasekar S, Design and Evaluation of Nifedipine Transdermal Patches, Indian journal of Pharmaceutical, Sciences, 2003, 65(5), 510-515.
32. Manvi F.V, Dandagi P.M, Gadad A.P, Mastiholimat V.S and Jagdeesh T, Formulation of Transdermal Drug Delivery System of Ketotifen Fumarate, Indian journal of Pharmaceutical Sciences, 2003, 65(3), 239-243.
33. Bharkatiya M, Nema R.K, Bhatnagar M, Designing and Characterization of Drug free patches for Transdermal Application, IJPSDR 2010, 2(1), 35-39.
34. Yuveraj Singh Tanwar, Chetan Singh Chauhan, Anshu Sharma, Development and Evaluation of Carvidilol Transdermal Patches, Acta Pharm, 2007,57, 151– 159.
35. Diveyesh Patel, Nirav Patel, Meghal Parmar, Transdermal Drug Delivery System, Review, International Journal of Biopharmaceutical and Toxicological Research,2011,1(1),61- 80.
36. Deepak Gondaliya and Kilambi Pundarikakshudu, Studies in Formulation and Pharmacotechnical Evaluation of Controlled Release Transdermal Delivery System of

Bupropion, AAPS Pharmscitech, 2003, 4 (1), 1-9.

37. Vamshi Vishnu Y, Chandrasekhar K, Ramesh G and Madhusudan Rao Y, Development of Mucoadhesive Patches for Buccal Administration of Carvedilol, Current Drug Delivery, 2007, 4, 27-39.
38. Amnon C, Sintov, Igor Krymberk, Vladimir Gavrilov and Rafael Gorodischer, Transdermal Delivery of Paracetamol for Paediatric use, effects of vehicle formulations on the percutaneous penetration, Journal of Pharmacy and Pharmacology, 2003, 55, 911-919.
39. Ayman el-kattan, Charles, S, Asbill and sam haidar, transdermal testing, practical aspects and methods, PSTT, 2000, 3(12), 426- 430.
40. Samir D, Roy and Elizabeth Manoukian, Transdermal Delivery of ketorolac Tromethamine, Permeation enhancement, Device Design, and Pharmacokinetics in Healthy Humans, Journal of Pharmaceutical Sciences, 1995, 84 (10), 11901199.
41. Rajeev Gokhale, Cynthia Schmidt, Lisa Alcorn, James Stolzenbach, Transdermal Drug Delivery Systems of Albuterol, In Vitro and In Vivo Studies, Journal of Pharmaceutical Sciences, 1992, 81(10), 996-999.
42. Deepak Gondaliya and Kilambi Pundarikakshudu, Studies in formulation and pharmacotechnical evaluation of Controlled Release Transdermal Delivery System of Bupropion, AAPS PharmSciTech, 2003, 4(1), 1-9.
43. Dhiman Sonia (2011) Transdermal Patches: A Recent Approch To New Drug Delivery System. International Journal of Pharmacy and Pharm 3(5)
44. Arti Kesarwani, Ajit Kumar Yadav, Sunil Singh,Hemendra Gautam, Haribansh N. Singh, Anamika Shvarma, Chitresh Yadav. A review – Theoretical aspects of Transdermal Drug Delivery System. Bulletin of Pharmaceutical Research, 3(2), 2013, 78-89.
45. Sampath Kumar KP, Debjit Bhowmik and Chiranjib B, R M Chandira. A review-Transdermal Drug Delivery System - A Novel Drug Delivery System and its market scope and opportunities. International Journal of Pharma and Bio Sciences, 2010, 1(2),1-21.
46. Soni S and Dixit V K. Transdermal delivery system. Indian Drugs, 29(11), 1992, 466-467.
47. Panchagnula R. Transdermal delivery of drugs. Indian Journals Pharmacology, 29(2), 1997, 140-56.
48. Vyas S P and Khar R K. Targeted and controlled Drug Delivery Novel carrier system, CBS Publishers and distributors, New Delhi, (2-Volume set), 1st Edition, 2002, 411- 447.
49. Marc B Brown, Matthew JT, Gary PM and Franklin KA. Transdermal drug delivery systems. Skin perturbation devices.1-32.
50. Prausnitz MR. Microneedles for transdermal drug delivery. Advance Drug Delivery Reviews, 56, 2004, 581-587.
51. Jain A, Mishra A, Nayak S and Soni V. Transdermal delivery of antihypertensive agents: A tabular update. International Journal of Drug Delivery, 3, 2011, 1-13.
52. Sharma N, Aggarwal G, Rana AC, Bhat Z and Kumar D. A Review: Transdermal drug delivery system: A tool for novel drug delivery system. International Journal of Drug Development and Research, 3, 2011, 70-84.
53. Sampath Kumar KP, Debjit B, Chiranjib B and Chandira RM. Transdermal drug delivery system- a novel drug delivery system and its market scope and opportunities. International Journal of Pharmacy and Bio Sciences, 1, 2010, 1-21.